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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,586	10/17/2001	George A. Gaitanaris	50001/002005	7567

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

QIAN, CELINE X

ART UNIT PAPER NUMBER

1636

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/982,586

Applicant(s)

GAITANARIS, GEORGE A.31 C

Examiner

Celine X Qian

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-13,18 and 20-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-13,18 and 20-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/24/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 2, 6-13, 18, 20-24 are pending in the application.

This Office Action is in response to the Amendment filed on 9/24/04.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/04 has been entered.

Response to Amendment

The rejection of claims 5-7 under 5 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection to 1, 2, 6-13, 18 under 35 U.S.C. 103 (a) has been withdrawn in light of Applicant's amendment of the claims.

Claims 1, 2, 6-13, 18 and newly added claims 20-24 stand rejected under 35 U.S.C. 112 1st paragraph for reasons set forth of the record mailed on 3/22/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1636

Claims 1, 2, 6-13, 18 and newly added claims 20-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicant argues the specification did teach how to use the claimed mice regardless whether there is a readily identifiable phenotype, in methods such as conditional ablation of cell lineages expressing mutant genes, spatiotemporal phenotypic analysis of disrupted genes, and conditional expression of genes of interest. Applicant argues that the office's concern about a readily identifiable phenotype in the claimed mouse is unwarranted since the invention is any mouse having two transgenes recited in the claims. Applicant asserts that a phenotype is neither required by the claims nor would be appropriate to require a particular phenotype since the phenotype will depend in each case on which endogenous gene is subject to the integration event and which second transgene is employed. Moreover, Applicant points out that the lack of a described phenotype is not relevant to the enablement of the claims. Applicant argues that a mouse having a mutation in an endogenous gene but resulting no phenotype is of interest because of its lack of phenotype. Applicant asserts that such mouse can be used to study the expression pattern of the mutated endogenous gene by using a gene encoding a reporter such as GFP. Applicant further asserts the claimed mouse can be used to study the ability of a gene to complement a mutated gene. Applicant thus conclude that a phenotype is not required for the enablement of the instant claimed invention.

Art Unit: 1636

These arguments have been fully considered but deemed unpersuasive. The reasons for non-enablement of the claimed invention is discussed in detail in the previous office action mailed on 7/2/03 and 3/22/04. In response to Applicant's argument regard no phenotype is required for the enablement of the claimed invention, the examiner respectfully disagree with this assertion. Applicant is reminded that the statute of 112 1st paragraph requires that the specification contain a written description of the claimed invention in full, clear, concise and exact terms to enable one of skilled in the art to make and use the claimed invention without undue experimentation. As discussed in the previous office action, the prior art teaches that the phenotype of the transgenic animal is unpredictable because of the influence of the genetic background such as positional effects (which would influence the expression of said gene), and the strength of the promoter of the endogenous gene. As such, one cannot predict the phenotype of a transgenic mouse based on a genotype, such as having two transgenes integrated into the genome of the mouse. Without teaching from the specification, whether the first transgene can be expressed at high enough level so that it can interact with the regulatory region of the second transgene is unpredictable. Even if the first transgene encoding transcription factor is expressed at high enough level such it can interact with the regulatory sequence of the second transgene, however, it still cannot predict whether the second transgene can be expressed at a high enough level to produce a phenotype, and such phenotype is necessary for methods taught by the instant specification such as cell lineage ablation, spatiotemporal phenotypic analysis of the disrupted gene and conditional expression of the gene of interest. Contrary to Applicant's assertion, a phenotype is necessary to enable the embodiments taught by the instant specification. Without a phenotype, one of skilled in the art would not know how to use the claimed invention for

Art Unit: 1636

methods of cell lineage ablation, spatiotemporal phenotypic analysis of the disrupted gene and conditional expression of the gene of interest. Since the specification does not teach a phenotype for the claimed mouse and the prior art considers the phenotype for transgenic mouse as unpredictable, one of skilled in the art would have to engage in undue experimentation to make and use the claimed invention.

In response to Applicant's argument regarding use of the mouse for studying the expression pattern of the endogenous gene by using a gene encoding a reporter such as GFP, the examiner still considers a phenotype such as expression of the first and second transgene at high enough level is necessary for this utility. For reasons discussed above, it is unpredictable whether this can be achieved without teaching from the specification. In response to Applicant's argument of using the mouse to study whether a gene complements the endogenous gene, the same rationale would apply. If the expression of the transgene is unpredictable, one skilled in the art would not know whether the "non-phenotype" is result from is result from complementation of the second transgene, non expression of the first gene, or non expression of the second gene without undue experimentation. As such, the claimed invention is not enabled for reasons discussed in the previous actions and above. This rejection is thus maintained.

Newly added claims 20-24 are rejected for same reasons as discussed above.

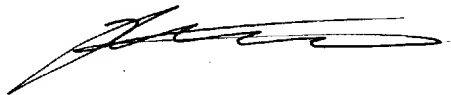
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

Art Unit: 1636

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

A handwritten signature in black ink, appearing to read 'Celine X Qian', with a stylized flourish at the end.